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Award Number: W81XWH-06-1-0765

TITLE: Automation and Preclinical Evaluation of a Dedicated Emission Mammotomography System for Fully 3-D Molecular Breast Imaging

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REPORT DATE: October 2008

TYPE OF REPORT: Annual Summary

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
Distribution Unlimited

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE 1 Oct 2008	**2. REPORT TYPE** Annual Summary	**3. DATES COVERED** 15 Sep 2007 – 14 Sep 2008
4. TITLE AND SUBTITLE Automation and Preclinical Evaluation of a Dedicated Emission Mammotomography System for Fully 3-D Molecular Breast Imaging		**5a. CONTRACT NUMBER**
		5b. GRANT NUMBER W81XWH-06-1-0765
		5c. PROGRAM ELEMENT NUMBER
6. AUTHOR(S) Spencer J. Cutler E-Mail: spencer.cutler@duke.edu		**5d. PROJECT NUMBER**
		5e. TASK NUMBER
		5f. WORK UNIT NUMBER
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Duke University Durham, NC 27710		**8. PERFORMING ORGANIZATION REPORT NUMBER**
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012		**10. SPONSOR/MONITOR'S ACRONYM(S)**
		11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

The overall objective of this proposal is to fully automate and optimize the performance of a 3-D dedicated emission mammotomography system for enhanced semi-automated clinical testing. In the second year of study, automated laser-guided contouring hardware and software were successfully implemented, and a final design is in progress. An observer-based direct comparison of 3D dedicated SPECT and 2D planar scintimammography was also conducted. Measuring estimated volumes by voxel integration of the MRI images expanded the retrospective MRI study from Year 1. Limited angle SPECT and CT were investigated in an effort to image a greater portion of the breast. As part of the training program and in progress toward obtaining a doctoral degree, I successfully passed my preliminary exam and obtained a Master's Degree.

15. SUBJECT TERMS
Nuclear Medicine Imaging, SPECT, Molecular Breast Imaging, Mammotomography

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION OF ABSTRACT**	**18. NUMBER OF PAGES**	**19a. NAME OF RESPONSIBLE PERSON** USAMRMC
a. REPORT U	**b. ABSTRACT** U	**c. THIS PAGE** U	UU	24	**19b. TELEPHONE NUMBER** *(include area code)*

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Introduction

The overall objective of this proposal is to fully automate and optimize the performance of a 3-D dedicated emission mammotomography system for enhanced semi-automated clinical testing. The main hypothesis of this work is that 3-D automated molecular breast imaging, with the ability to dynamically contour any sized breast, will improve detection and potentially in vivo characterization of small (<1cm) early stage breast cancer and provide a patient-friendly imaging modality ready for clinical testing. In the second year of this research, automated laser-guided contouring functional prototype hardware and software were successfully implemented with more sophisticated designs in progress. Building on earlier work, an observer based study directly comparing 3D dedicated SPECT and 2D planar scintimammography was also conducted. Limited angle SPECT and CT were investigated in an effort to image a greater portion of the breast. I successfully passed my preliminary exam in progress toward obtaining a doctoral degree, and obtained a Master's Degree.

Body

Task 1. Conduct a retrospective study of breast volumes, shapes, and sizes using existing anonymized bilateral MRI breast data (Refer to Appendix A for original statement of work):

In the first year of study, a retrospective study of 103 clinical MRI uncompressed breast scans was conducted to create surface renderings of the uncompressed breasts and analyze how to adapt existing acquisition orbits for varying breast shapes. After consultation with Radiology residents on how and where to make measurement form the MRI images, measured parameters included nipple-to-chest wall (mean=8.2cm), superior-inferior (mean=10.5cm), and medial-lateral distances (mean=14.1cm) (Fig. 1). In year two, estimated volumes of the breasts were calculated by first segmenting the images and then using mesh voxel integration of the MRI images (Fig 1). The mean measured volume was ~700mL. With this result, future breast phantom experiments should utilize ~700mL breast volumes as previous experiments in our lab have mainly used phantoms >1000mL in volume, under the assumption that larger breasts are more difficult to image. This work was presented at the both the *2008 DOD Era of Hope Meeting* (Appendix E) and at the *2008 IEEE Medical Imaging Conference* in Dresden, Germany.

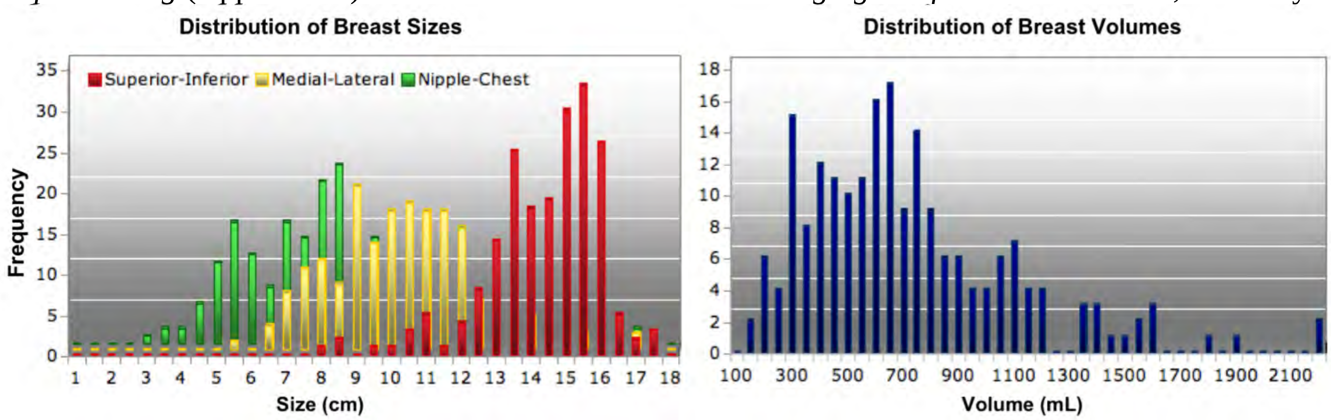

Fig. 1. Frequency distributions of measured breast parameters extracted from 202 individual MRI breast volumes. Breast volumes were estimated using segmentation and mesh volume calculations. The measured MRI breast sizes from this study retrospectively validate the range of shapes and sizes (250 to 1700 mL volumes) of custom shaped pendant breast phantoms available in the MMI Lab at Duke for preclinical research purposes.

Task 2. Implement 3-D fully automated contouring orbits for dedicated SPECT breast imaging:

The dedicated breast CZT-based SPECT imaging system in our lab implements novel 3-D camera trajectories that minimize breast-detector separation, thus improving resolution and image quality. These trajectories are currently customized for each patient by manually measuring breast-detector separations at several positions and interpolating between them. This task seeks to transition from this manual method to a quicker and more robust automated contouring solution for routine patient SPECT imaging, given the vast array of uncompressed breast shapes in women.

In Year 1, low divergence, ribbon laser feedback sensors (*Keyence*, 4cm wide lasers (model LV-51M) and detectors (LV-H300)) were purchased and proof-of-principle bench tests with the ribbon lasers were successfully completed, measuring a change in beam intensity even using clear breast phantoms.

In Year 2, a working prototype was completed, allowing for dynamic laser-guided contouring for the SPECT system (Fig 2). First, a circuit was designed and built to power the sensor amplifiers and to channel the output receiver voltages (feedback) into the analog-to-digital converter of the Newport motion controller (ESP7000). The data acquisition and motion control software was then modified to read in the digitized signals, and new algorithms were created to position the camera based on the feedback from the lasers. The camera radius is thereby adjusted within ~1.5cm of the breast surface, but no closer than 0.5cm, thus safely keeping the camera face as close to breast as possible in a contoured trajectory.

Second, a 2x2 array of transmitter-receiver laser pairs were mounted on a thin piece of acrylic plastic, effectively creating two virtual planes with independent upper and lower positional data in each plane (Fig. 2, LEFT). After bench-top tests, this plastic sheet was adhered to the face of the SPECT camera. Using the functional prototype, we were able to automatically contour a 700mL breast phantom with no initial setup time. Trajectory repeatability for a fixed breast phantom was found to be very high, with only a few slight differences of less than 1mm over multiple measurements. Compared to a manually defined contour with the lasers, the automated approach kept the camera significantly closer during the scan (Fig. 3).

In Year 3, a fixed final hardware design will be completed with the sensors mounted vertically on the sides of the camera (Fig. 4) and then reflected across the face in order to minimize obstruction of the protruding sensors. Overall we have successfully implemented a working prototype for dynamic contouring, which has been shown to both simplify and expedite the overall SPECT imaging process. Automated orbits are highly robust, repeatable, and improve overall image quality. The completed implementation of dynamic laser-guided contouring will facilitate a smoother scanning process for ongoing clinical patient studies in the Duke Multi-Modality Imaging Laboratory.

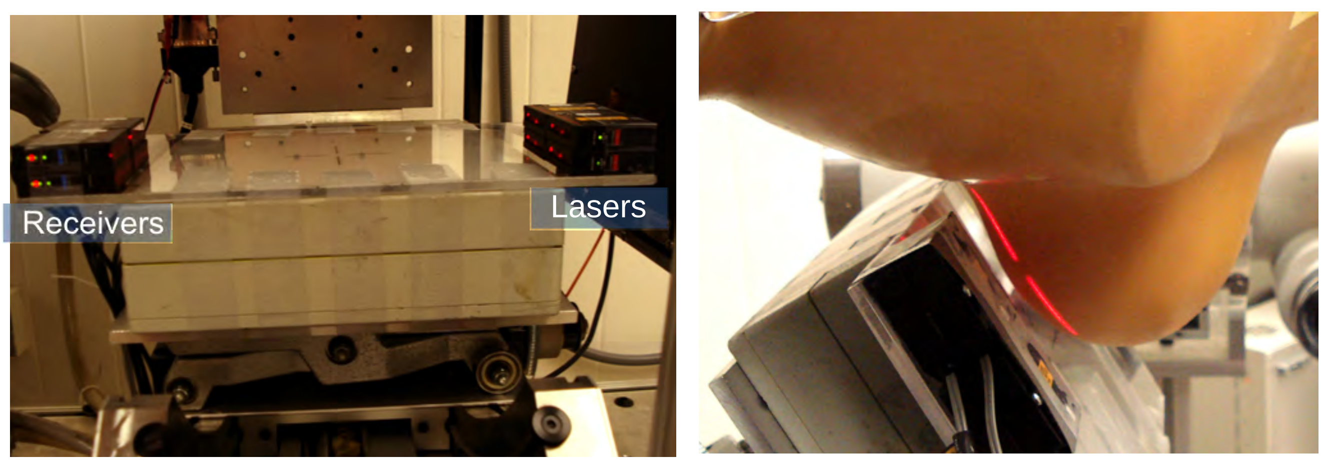

Fig. 2. (LEFT) Dual-layer prototype ribbon laser *(Keyence* Model HV300*)* contouring system attached to face of the SPECT camera. Sensor outputs are channeled through an ADC into the gantry motion controller (*Newport* ESP7000) that monitors and adjusts the ROR accordingly. (RIGHT) Separate 35mm wide top-layer ribbon laser beams are seen on the breast phantom skin, as the camera dynamically contours at a minimal radius or rotation to improve resolution and image quality.

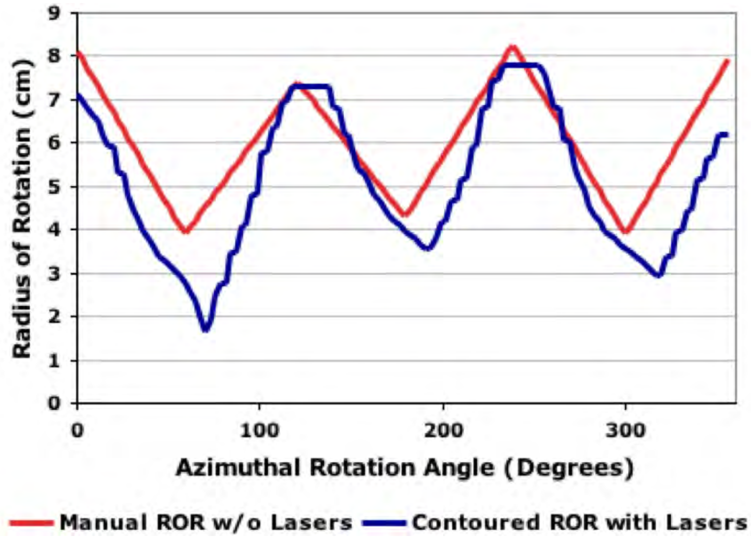

Fig. 3. 360^{o} SPECT radius-of-rotation (ROR) trajectories about a 700mL breast phantom. Laser guided contouring (blue) keeps the camera significantly closer to the breast (smaller ROR is better) during the scan compared to the manually created orbit (red)

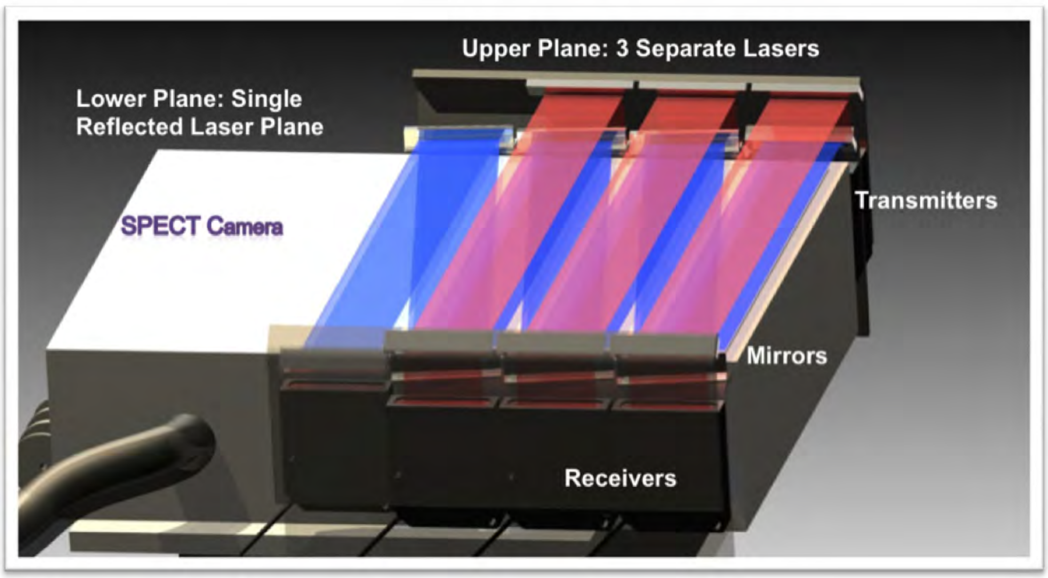

Fig. 4. Computer model of a future mounting design with the sensors mounted vertically to save space. The upper sensor layer (red) identifies the region on the camera face that has been penetrated, while the lower layer (blue) consists of a single, multiply reflected beam.

Task 3. Compare performance of the fully automated 3-D SPECT system with 2-D scintimammography:

The overall goal of Task 3 is to quantitatively and qualitatively compare 2D planar scintimammography (SCINTI) imaging of the breast under various degrees of compression with uncompressed, dedicated 3D SPECT using contoured acquisition trajectories through a limited observer study. As far as we are aware, this has not been done experimentally for 3D dedicated SPECT breast imaging. A 700mL compressible anthropomorphic breast phantom containing small lesions was utilized to compare 2D and 3D breast imaging (Fig. 5). Thin walled, deformable lesions from 40 to 500uL volume were arranged and suspended on a thin plastic sheet placed in the breast phantom were used to mimic breast lesions undergoing different degrees of compression. Using our 16x20cm^2 CZT-based gamma camera, ^{99m}Tc-scintimammography was performed for 10min imaging times for compression thicknesses from 6 to 12cm (fully uncompressed) using a single mediolateral view. Dedicated breast

SPECT was then performed for 10min using the uncompressed breast acquired with a simple tilted parallel beam rotation (TPB) and a complex 3D acquisition trajectory (PROJSINE). Experimental variables included background breast composition (Fig. 6-7), and low count (clinically relevant) and high count (low noise) images (Fig. 8). The radioactivity Lesion:Background concentration ratio was varied from 12:1 down to 3:1. A comparison between the two modalities was made in a limited observer study with 6 independent observers (2 nuclear medicine physicians and 4 medical physicists) analyzing reconstructed images for the smallest detectable lesion in these signal-known-exactly (SKE) cases. Image quality, based on lesion SNRs and contrasts, and sampled breast volume were also evaluated.

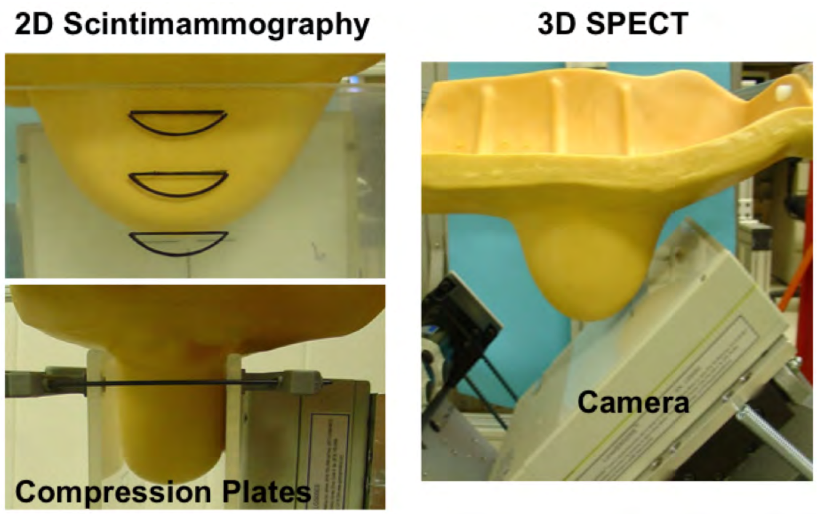

Fig. 5. (LEFT) Compressed 700mL breast phantom containing known lesions, and (RIGHT) Uncompressed SPECT set-up.

Due to greater positioning flexibility of the system gantry, dedicated SPECT was able to both image a larger breast volume and view the anterior chest wall, where tumors may be otherwise missed in 2D imaging. 3D SPECT and 2D SCINTI were generally statistically equivalent at 12:1, except that chest wall lesions were detected in SPECT that were not in the field of view of SCINTI. At 6:1 and 3:1, SPECT overall statistically outperformed SCINTI, seeing more and smaller lesions (Fig. 9). In the heterogeneous compressed breast SCINTI was equivalent to SPECT at 6:1. Clinical data seems to indicate that a 20min SPECT scan would be preferable to 10min to lower noise and boost sensitivity. Under a wide range of measurement conditions: More lesions, smaller lesion sizes, and (3D) lesion locations can be detected with dedicated emission mammotomography than with compressed breast scintimammography. Full methods and results will be included in the Year 3 final report, as the data needs further analysis.

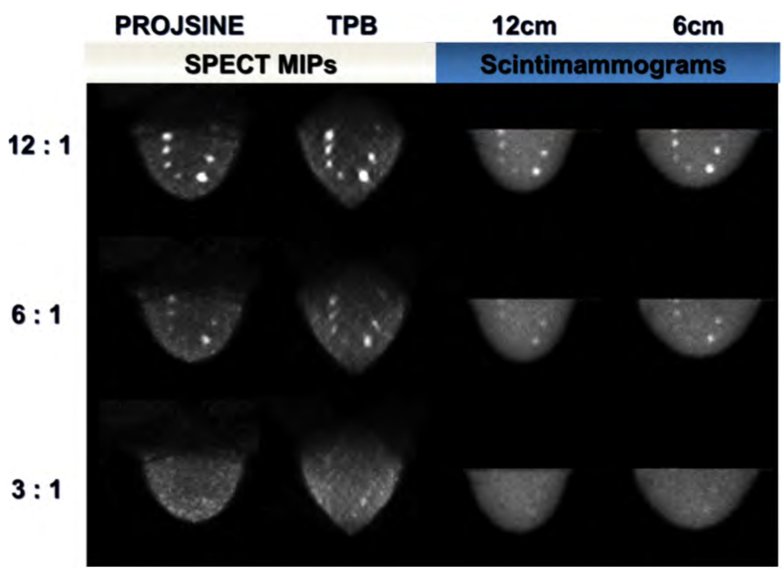

Fig. 6. Iteratively reconstructed (8 subsets, 1 iteration) SPECT maximum intensity projections (MIPs) shown together with uncompressed (12cm) and compressed (6cm) scintimammograms acquired of the same breast phantom for varying lesion to background concentrations.

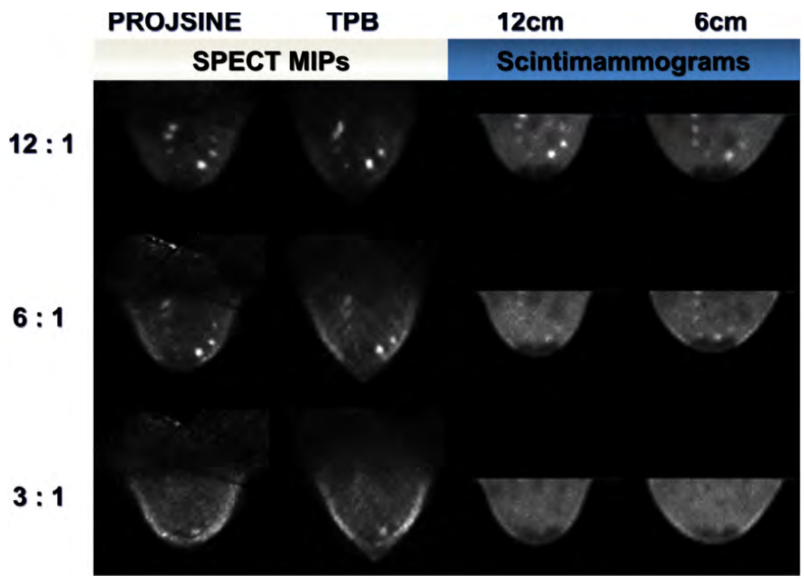

Fig. 7. Iteratively reconstructed (8 subsets, 1 iteration) SPECT MIPs shown next to scintimammograms acquired of the same breast phantom now with added attenuating material to simulate non-uniform uptake in the breast background.

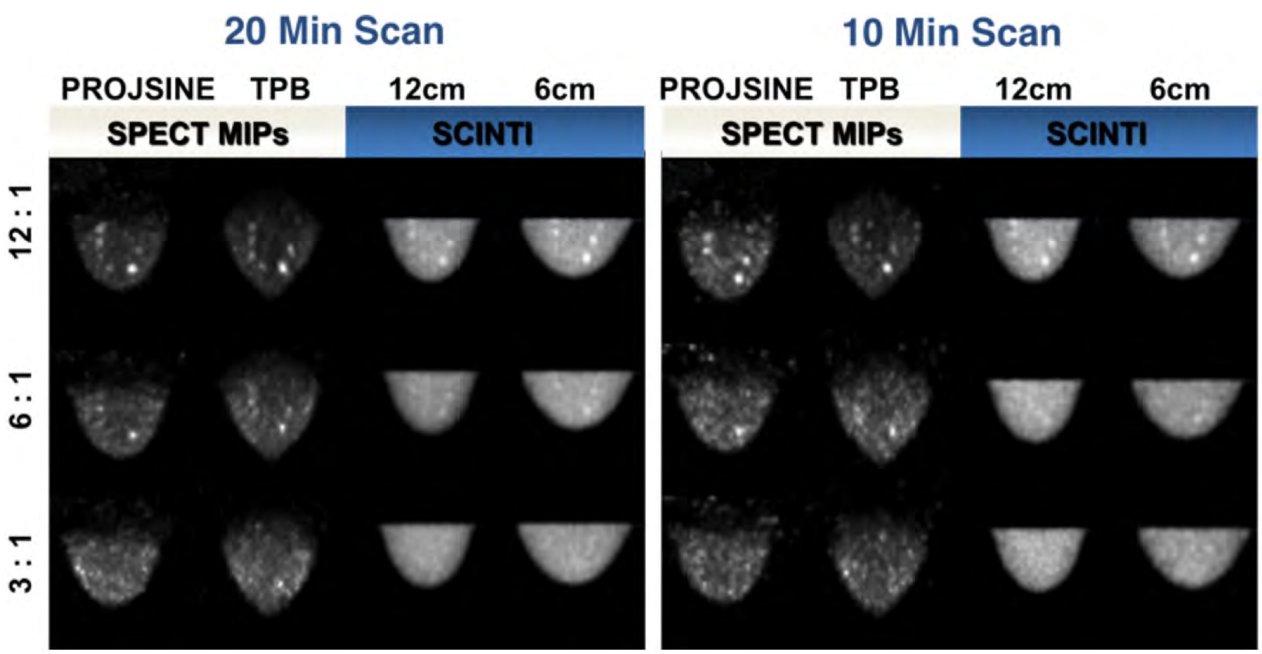

Fig. 8. Collected list-mode data were down-sampled to simulate count levels of 20 minute and 10 minute clinical scan.

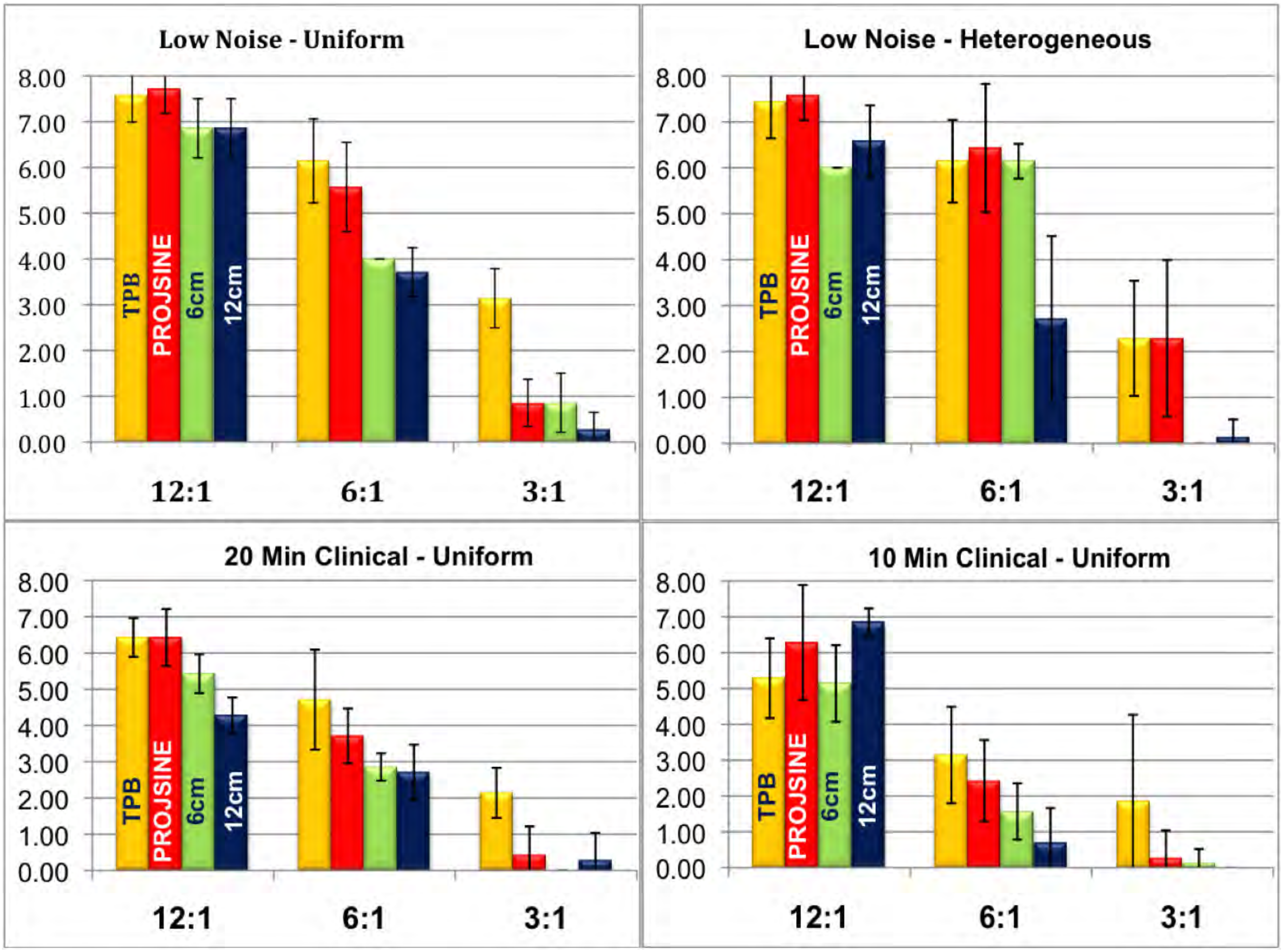

Fig. 9. Initial observer results showing number of lesions observed on the y-axis and lesion to background ratio on the x-axis. Standard deviation over 7 observers is displayed. The top row compares a uniform breast background with a heterogeneous breast background. The bottom row compares simulated 20-minute vs. 10-minute clinical count level scans. In general, SPECT (TPB and PROJSINE) are statistically equivalent at 12:1. At 6:1 and 3:1, SPECT outperforms SCINTI.

Task 4. Complete other aspects of breast cancer training program:

In March of 2008 I successfully passed my preliminary exam using much of the research from this predoctoral award as the basis of my proposed thesis, "Preclinical Evaluation of a Dedicated SPECT-CT Mammotomography System for Quantitative Hybrid Breast Imaging." The preliminary exam consisted of submitting a 30-page NIH grant-format proposal and research summary, and then a three-hour oral examination discussing the proposed work. I also received a Master's of Engineering degree in biomedical engineering independent of the process of the examination.

Key Research Accomplishments

Year 2 included Tasks 2-4 from the original Statement of Work (Appendix A), with one addition to the previously completed Task 1:

- The MRI study proposed in Task 1 was revisited, calculating breast volumes and classifying each of the 202 individual breasts in the database (mean volume = 700mL).

- A working prototype dynamic laser-guided contouring system for the SPECT system was completed and found to significantly simplify the complex imaging. Final mounting hardware designs are in progress. This research was accepted for presentation at the *2008 IEEE Nuclear Science Symposium & Medical Imaging Conference,* and a conference proceeding and peer-reviewed paper are in progress.
- A significant portion of Task 3 was completed ahead of the proposed timeline. A limited observer study was conducted comparing 3D dedicated breast SPECT and 2D scintimammography. This research was accepted for presentation at the *Fourth International Workshop on the Molecular Radiology of Breast Cancer (MRBC),* and a conference proceeding and peer-reviewed paper are in progress.
- I passed my preliminary exam in progress toward obtaining a doctoral degree and as part of the training program in Task 4.
- Limited angle SPECT and CT were investigated in an effort to image a greater portion of the breast. These results were presented at the *2007 IEEE Nuclear Science Symposium and Medical Imaging Conference*, 30 October – 3 Nov., Honolulu, Hawaii (Appendix B).
- I contributed work to nine additional presentations made at the *2008 DOD Era of Hope, 2008 AAPM, 2008 MRBC Workshop,* and several local Duke conferences. A sampling of abstracts is included in Appendices C-F. Three first-author papers are in preparation for peer review.

Reportable Outcomes

Presentations, Published Abstracts, and Published Proceedings:

- **SJ Cutler**, DJ Crotty, P Madhav, KL Perez, MP Tornai. "Comparison of reduced angle and fully 3D acquisition sequencing and trajectories for dual-modality mammotomography." Presented at the *2007 IEEE Nucl. Sci. Symposium & Med. Imaging Conference*, Honolulu, Hawaii, 28 Oct.-3 Nov. 2007 and published in *IEEE Conference Record NSS/MIC*, 6:4044-4050.

- KL Perez, **SJ Cutler**, and MP Tornai, "Empirical effects of angular sampling and background content on image quality in dedicated breast SPECT," Presented at the *2007 IEEE Nucl. Sci. Symposium & Med. Imaging Conference*, Honolulu, Hawaii, 28 Oct.-3 Nov. 2007 and published in *IEEE Conference Record NSS/MIC.* 4:3065-3069.

- P Madhav, DJ Crotty, KL Perez, **SJ Cutler**, RL McKinley, TZ Wong, MP Tornai. "Initial patient study with dedicated dual-modality SPECT-CT mammotomography." Presented at the *2007 IEEE Nucl. Sci. Symposium & Med. Imaging Conference*, Honolulu, Hawaii, 28 Oct.-3 Nov. 2007 and published in *IEEE Conference Record NSS/MIC*, 5:3781-3787.

- P Madhav, **SJ Cutler**, DJ Crotty, KL Perez, RL McKinley, MP Tornai. "3D volumetric breast imaging with a dedicated dual-modality SPECT-CT system." Presented at the *2007 Duke Biomedical Engineering Retreat*, Myrtle Beach, SC, 7-9 Oct. 2007.

- DJ Crotty, P Madhav, **SJ Cutler**, KL Perez, RL McKinley, MP Tornai, "Performance of a new dual-modality molecular-anatomical imaging system dedicated to breast cancer." Presented at the *2008 Duke Cancer Center Annual Meeting*, Durham, NC, 10 Mar. 2008.

- P Madhav, **SJ Cutler**, DJ Crotty, KL Perez, RL McKinley, PK Marcom, TZ Wong, MP Tornai. “Dedicated molecular and anatomical breast imaging - initial patient studies.” Presented at the *2008 Duke Cancer Center Annual Meeting*, Durham, NC, 10 Mar. 2008.

- **SJ Cutler**, MP Tornai. “Automation and Preclinical Evaluation of a Dedicated Emission Mammotomography System for Fully 3-D Molecular Breast Imaging.” Presented at the 2008 DOD Era of Hope Conference on Breast Cancer, Baltimore, MD, 25-28 Jun. 2008.

- P Madhav, **SJ Cutler**, DJ Crotty, KL Perez, RL McKinley, PK Marcom, T Wong, MP Tornai. “Pilot Patient Studies Using a Dedicated Dual-Modality SPECT-CT System for Breast Imaging.” Presented at the *50th Annual Meeting of the American Association of Physicists in Medicine*, Houston, TX, 27-31 Jul. 2008.

- **SJ Cutler**, DJ Crotty, MP Tornai. “Dynamic Laser-Guided Contouring for Dedicated Emission Mammotomography.” Accepted for presentation at the *2008 IEEE Nuclear Science Symposium & Medical Imaging Conference*, Dresden, Germany, 19-25 Oct. 2008.

- **SJ Cutler**, KL Perez, P Madhav, MP Tornai. “Comparison of 2D Scintimammography and 3D Dedicated Breast SPECT Using A Compressible Breast Phantom and Lesions of Varying Size and Tracer Uptake.” Accepted for presentation at the *Fourth International Workshop on the Molecular Radiology of Breast Cancer (MRBC),* Dresden, Germany, 20 - 21 Oct. 2008.

- KL Perez, **SJ Cutler**, P Madhav, MP Tornai “Novel Patient Acquisition Trajectories for Optimized Dedicated Breast SPECT Imaging.” Accepted for presentation at the *Fourth International Workshop on the Molecular Radiology of Breast Cancer (MRBC),* Dresden, Germany, 20 - 21 Oct. 2008.

- DJ Crotty, **SJ Cutler**, P Madhav, KL Perez, RL McKinley, MP Tornai. “Improved Chest Wall Imaging through Combined Complex Trajectories in Dedicated Dual Modality SPECT-CT Breast Molecular Imaging.” Accepted for presentation at the *Fourth International Workshop on the Molecular Radiology of Breast Cancer (MRBC),* Dresden, Germany, 20 - 21 Oct. 2008.

Conclusions

Dynamic laser-guided SPECT contouring hardware and software were successfully implemented and have been shown to both simplify and expedite the overall SPECT imaging process. Automated orbits are highly robust, repeatable, and improve overall image quality. A direct comparison of 3D dedicated breast SPECT and 2D planar scintimammography was made with preliminary analysis of the data indicated that SPECT outperforms 2D planar imaging for this signal known exactly observer study. Significant progress has been made in Year 2, and all remaining tasks of the grant are on schedule to be completed in the final year of this predoctoral award.

Appendices

Appendix A
STATEMENT OF WORK

Task 1 Conduct a retrospective study of breast volumes, shapes, and sizes using existing anonymized bilateral MRI breast data (Months 1-4):

a. Acquire IRB approval to use already acquired MRI uncompressed breast data sets for 50-100 patients (Month 1).
b. Extract the pendant breast sizes: nipple-chest wall distance, superior-inferior distance, medial-lateral distance, skin thickness, and obtain a rendering of external breast surface shape (Months 1-4).
c. Tabulate metrics of distance measurements and classify the varying spectrum of pendant breast surfaces (Month 4).

Task 2 Implement 3-D fully automated contouring orbits for dedicated SPECT breast imaging (Months 3-16):

a. Based on the results of Task 1, modify the existing basis set of orbits to account for challenges imposed by non-uniform breast shapes (Month 4).
b. Develop and implement a series of optical or ultrasonic feedback sensors on the camera for dynamic contouring. Update software interface to implement real-time feedback from sensors (Months 3-12).
c. Investigate dynamic acquisition robustness using anthropomorphic breast phantoms of varying size and shape, and compare reconstructed image quality to images acquired previously using manually defined orbits (Months 13-15).

Task 3 Compare performance of the fully automated 3-D SPECT system with 2-D scintimammography (Months 15-36):

a. Characterize and optimize 3-D system using geometric phantoms and anthropomorphic breast and torso phantoms, acquiring data under various lesion-to-background concentration conditions, with and without patient shielding, and for a variety of automated complex orbits (Months 15-21).
b. Assess reconstructed images for contrast, signal-to-noise ratio, artifacts, and lesion detectability for both low noise and clinical high noise count rates (Months 22-25).
c. Utilize compressible breast phantom containing various lesions and in varying lesion-to-background ratios to acquire 2-D planar data under varying compressions for scintimammography as well as uncompressed breast 3-D tomographic imaging (Months 26-30).
d. Conduct a limited observer study to evaluate reconstructed images for smallest lesion detectability under varying contrasts, noise levels, background uniformity, and patient shielding conditions (Months 31-36).

Task 4 Complete other aspects of breast cancer training program (Months 1-36):

a. Clinical shadowing patients having breast cancer management (Nuclear Medicine Clinic, Mammography Clinic) (Months 1-12)
b. Publish research work in peer-reviewed journals. (Months 1-36)
c. Attend and present at local Duke Medical Center lectures and medical seminars related to breast cancer (Months 1-36)
d. Attend and present work at international conferences: *DOD BCRP Era of Hope Meeting*, *IEEE Medical Imaging*, *Society of Nuclear Medicine*, *Radiological Society of North America*, and *San Antonio Breast Cancer Symposium*. (Months 1-36).
e. Prepare for and defend thesis (Months 30-36)

APPENDIX B

IEEE 2007 Nuclear Science Symposium and Medical Imaging Conference Conference Record

Comparison of Reduced Angle and Fully 3D Acquisition Sequencing and Trajectories for Dual-Modality Mammotomography

Spencer J. Cutler, *Member, IEEE*, Priti Madhav, *Member, IEEE*, Kristy L. Perez, *Member, IEEE*, Dominic J. Crotty, *Member, IEEE*, Martin P. Tornai, *Senior Member, IEEE*

***Abstract*– A dual-modality SPECT-CT system for dedicated 3D breast cancer imaging is under development. Independent dedicated SPECT and CT imaging systems have been integrated onto a single gantry for uncompressed breast imaging. This study examines challenges and tradeoffs involved in integrating the acquisition procedures of two independent imaging systems into a single imaging protocol. The physical limitation of the rotating CT tube beneath the custom patient bed currently provides only a 294 degree scan with the bed low enough for the breast to be in the cone-beam CT field-of-view. The directly coupled SPECT system is therefore also limited if the scans are to be taken simultaneously or in an interleaved fashion. Thus, geometric phantoms are imaged to characterize image degradations due to reduced projection angles for both modalities. Two different acquisitions were performed: one with the central ray of the CT cone-beam aligned with the system's center of rotation and one offset from the center of rotation by 5cm. Various sized activity-filled lesions in an anthropomorphic breast phantom were imaged, first with uniform aqueous background activity and then with added acrylic pieces to simulate a non-uniform background. Interleaving the SPECT and CT acquisitions into a single scan was also investigated. Iterative reconstruction algorithms are used to reconstruct the data, and the SPECT and CT images are co-registered. Both the cold rod and breast data indicate that removing 75^{o} of SPECT azimuthal data does not significantly reduce image quality. CT images were also minimally affected if the cone-beam is centrally aligned with the center of rotation, but degraded with the laterally offset cone–beam setup. In the course of these experiments, the patient bed was reconfigured with a larger central hole covered with flexible neoprene, gaining the ability to rotate completely around the breast and dramatically improving CT projection views through the chest wall.**

I. Introduction

INDEPENDENT SPECT and x-ray CT subsystems developed in our lab have been integrated into a single system for pendant uncompressed, fully-3D multimodality breast imaging, providing co-registered volumetric anatomical and functional information [1]. A custom-designed patient bed was also developed with the goal of maximizing patient comfort while imaging close to the chest wall [2]. This study examines challenges and tradeoffs involved in integrating the acquisition procedures of two independent imaging systems into a single imaging protocol.

The benefits of simultaneous or interleaved SPECT-CT imaging include potentially shorter overall imaging times, simpler inherent image registration, and more straightforward SPECT attenuation correction using the corresponding CT data. Consecutive scans benefit from improved and more uniform 3D SPECT resolution and sampling. Emission contamination of the CT images can also be avoided by acquiring the CT scan prior to radionuclide injection of the patient [3].

Reduced or limited angle tomography has been investigated for both emission and transmission breast imaging [4-9]. These studies usually involve limited circular imaging trajectories of less than 180 degrees. Our objective is to qualitatively examine the tradeoffs of removing a much smaller portion of the full 360 degree azimuthal imaging arc. The SPECT component of our system also introduces the question of how reduced angle tomography affects complex 3D imaging trajectories [10, 11].

II. Materials & Methods

Specifics and materials of the individual subsystems, combined hybrid SPECT-CT system, as well as the patient bed have been detailed previously [1, 2, 12, 13].

The physical limitation of the rotating CT tube beneath the custom patient bed, combined with the dead edge at the top of the CT detector, currently prevents a full 360 degree dual-modality scan with the bed low enough for the breast to be fully in the cone-beam CT field-of-view (FOV). To increase the volume of the breast in the FOV, the bed was lowered and projection images were acquired at a reduced number of angles (~294 degrees) about the breast, avoiding the head rest of the patient (Fig. 1). The directly coupled SPECT system is therefore also limited in motion if the scans are taken simultaneously in the common FOV. Alternatively, following a reduced angle CT scan, a separate SPECT scan can be made by fixing the SPECT system center of rotation (COR) higher

Manuscript received November 23, 2007. This work was supported by the National Cancer Institute of the National Institutes of Health (R01-CA096821) and in part by the Department of Defense Breast Cancer Research Program (W81XWH-06-1-0765 and W81XWH-06-1-0791) and IEEE Student Travel Award.

The authors are with the Department of Radiology at Duke University Medical Center, Durham, NC 27710. S.J. Cutler, P. Madhav, D.J. Crotty, and M.P. Tornai are also with the Department of Biomedical Engineering at Duke University, Durham, NC 27708. K.L. Perez and M.P. Tornai are also with the Medical Physics Graduate program at Duke University Medical Center, Durham, NC 27710 (email:spencer.cutler@duke.edu).

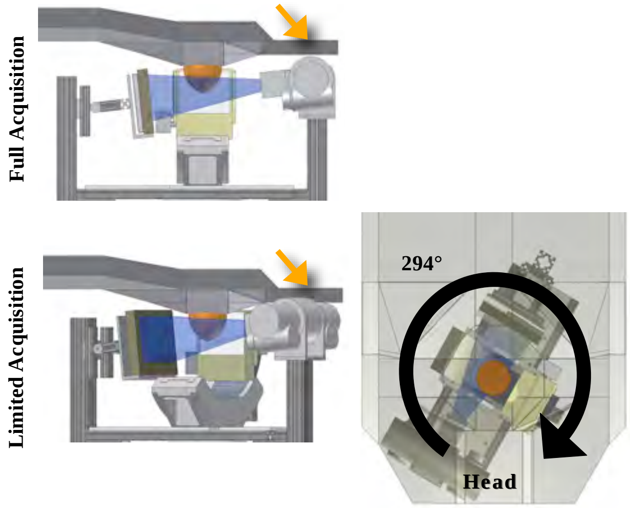

Fig 1: 3D CAD drawings of a (TOP) full and (BOTTOM) limited acquisition setup. The trough for the head (shown by the orange arrow) and physical dimensions of the x-ray tube limit the amount of breast volume in the FOV with a 360º scan, in contrast to a 294° acquisition where the breast can be further dropped into the FOV.

than the CT system and raising the bed to allow a 360^o clearance of the CT tube and detector.

A. *Geometric Phantom Study*

A mini-cold rod phantom (model ECT/DLX-MP, *Data Spectrum Corp.*, Hillsborough, NC) placed in a 7.7cm inner diameter cylinder was first used to characterize reduced angle tomography for both the SPECT and CT systems. The 2.6cm long rods were arranged in six sectors of equal diameters of 4.7, 3.9, 3.1, 2.3, 1.5, and 1.1mm, on a pitch of twice their diameters. 9.5mCi of ^{99m}Tc in water filled the interstitial spaces. The phantom was suspended vertically with the mini-rods in the center of the camera's field of view and parallel to the camera surface.

Data were acquired on the independent SPECT system using a simple 128 projection vertical-axis-of-rotation (VAOR) orbit over 360^o, acquired for 27 seconds per projection. This yielded a count rate of ~3.5kcounts/sec or approximately 95k counts per projection (in a ±4% energy window). List-mode data from the full 360^o acquisition were then post-processed by removing projections to simulate reduced angle acquisitions of 180^o, 240^o, and 300^o. The list-mode projection data were also truncated such that the total number of counts over the entire acquisition remained the same in an effort to make a time-normalized comparison of the varying reduced angle trajectories. SPECT data were reconstructed using an ordered subsets emission iterative algorithm [14]. Reconstructions were performed using a $2.5mm^3$ voxel size on a 150x150x150 grid, using 8 subsets, and 20 iterations.

With a source-to-image distance (SID) of 55cm, a source-to-center-of-object distance (SOD) of 35cm, and a COR to detector distance of 20cm, CT scans of the cold rod phantom were acquired at a tube potential of 60 kVp using a Ce 100th attenuating value layer (0.0508cm) filter (Z=58, r=6.77g/cm3, K-edge=40.4keV, *Santoku America, Inc.*, Tolleson, AZ) to

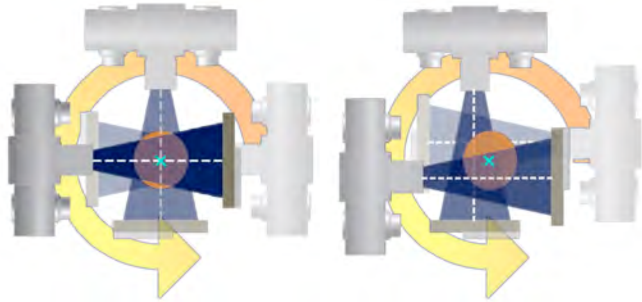

Fig. 2. (LEFT) Schematic illustrating the CT system with central ray of the cone-beam (white dashed line) aligned with the COR (blue x). This setup results in truncation of larger breasts (>15cm in diameter). (RIGHT) Schematic illustrating the advantage of the 5cm offset half-cone-beam used to acquire data for larger breast volumes.

yield a mean energy of ~36keV and FWHM of 15%. Two scans were performed for each set of phantoms: one with the central ray of the cone beam intersecting the axis of rotation (Fig. 2, LEFT), and one with the central ray offset 5cm laterally from the axis of rotation (Fig. 2, RIGHT). The centrally aligned setup results in truncation of larger breasts (>15cm in diameter) and therefore, a 5cm offset cone-beam is currently used in order to acquire data for larger breast volumes [15]. Data were acquired over 360^o in 1.5^o increments with VAOR. Reduced angle CT realizations of 180^o, 240^o, and 300^o were created by removing raw data projections. CT data were reconstructed using an ordered subsets transmission iterative algorithm [16]. Reconstructions were performed on 4x4 pixel binned image data (equaling a 0.508 mm voxel size) on a 350x350x384 reconstruction grid, using 16 subsets, and 10 iterations.

B. *Breast Phantom with Homogeneous Background*

A 900mL water-filled breast phantom with three lesions (2.7cm, 1.6cm, and 0.8cm outer diameter, with corresponding 2.3mL, 1.0mL, and 0.35mL volumes) were acquired on the SPECT and CT sub-systems. Each lesion was filled with ^{99m}Tc, with an absolute ratio of 20µCi/mL and ~50µL of CT contrast agent, Gastrografin with iodine (I_2). The lesion:background concentration ratio was 10:1. SPECT projections were acquired using a three-lobed sinusoid projected onto a hemisphere (PROJSINE) with polar tilting range (sinusodial amplitude) from 15 to 45° (Fig. 4, BOTTOM) and CT images were acquired using a fixed 6.2° tilt. The SID was increased to 60 cm, a SOD of 38.1 cm, and a COR to detector distance of 22 cm. This resulted in the same magnification of 1.57 for an object at the system's COR as the independent CT system mentioned in the earlier section. Tube potential and filtration remained the same as the previous study, and the CT system retained the 5cm lateral offset. A ±4% energy window symmetric about the 140keV photo peak was used for the all of the SPECT projections in these studies. Total scan time was ~10 minutes. List-mode data from the full 360^o acquisition were again count-normalized between the scans and cropped to create SPECT acquisitions of 180^o, 240^o, and 300^o. Corresponding CT data were also created by removing raw data projections.

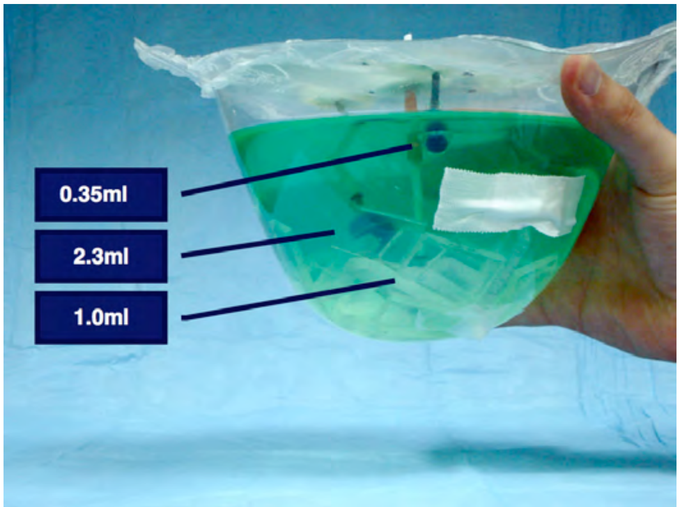

Fig. 3. Breast phantom filled with 900mL of aqueous ^{99m}Tc. Various-sized pieces of acrylic were added to the background to create a heterogeneous background and simulate non-uniform uptake in the SPECT images. Lesion locations and sizes are indicated in the figure.

SPECT reconstruction parameters were set to 3 iterations, 8 subsets, 150x150x150 reconstruction grid, and 2.5mm^3 voxel size. CT reconstruction parameters were set to 5 iterations, 16 subsets, 350x350x384 reconstruction grid, and 508µm^3 voxel size.

C. Breast Phantom with Heterogeneous Background

Small acrylic pieces were added to the same 900mL filled breast to simulate non-uniform uptake in the breast background (Fig. 3). Each lesion was again filled with ^{99m}Tc, with an absolute ratio of 21.8µCi/mL and ~50µL of CT contrast agent (Gastrografin). An activity-filled anthropomorphic heart was also placed above the breast to simulate cardiac uptake and contamination. The lesion:background:heart ratio was 10.8 : 1 : 6.1. Four 6.0mm nylon spheres (*Small Parts, Inc*, Miramar, Fl) were soaked in concentrated aqueous ^{99m}Tc and taped to the exterior surface of the breast phantom to act as fiducial markers for registration purposes.

Two dual modality acquisition sequences were tested with the filled breast phantom: 1) Reduced angle CT and SPECT acquisitions at a single patient bed height, and 2) separate, full 360^o CT and SPECT, each at varying bed heights.

For the first imaging sequence, the patient bed was lowered to the minimal height that the CT tube and detector could still pass beneath the torso of the patient, thereby maximizing the breast volume in the FOV for the rigid bed design. At this height the CT scan is limited to 294^o by the head trough of the bed (Fig 1). CT projections were acquired in 1.5^o increments. Reduced angle SPECT data were then acquired using three trajectories: a tilted-parallel-beam with 45° polar tilt (TPB45), a "Saddle" orbit, and a 3.5-lobed PROJSINE (Fig. 4, CENTER COLUMN). With the bed at minimal position optimized for the reduced angle CT scan, the SPECT polar tilting is limited to a range from 30° to 45°. Reduced angle acquisitions were made with 119 projections over 294° with a

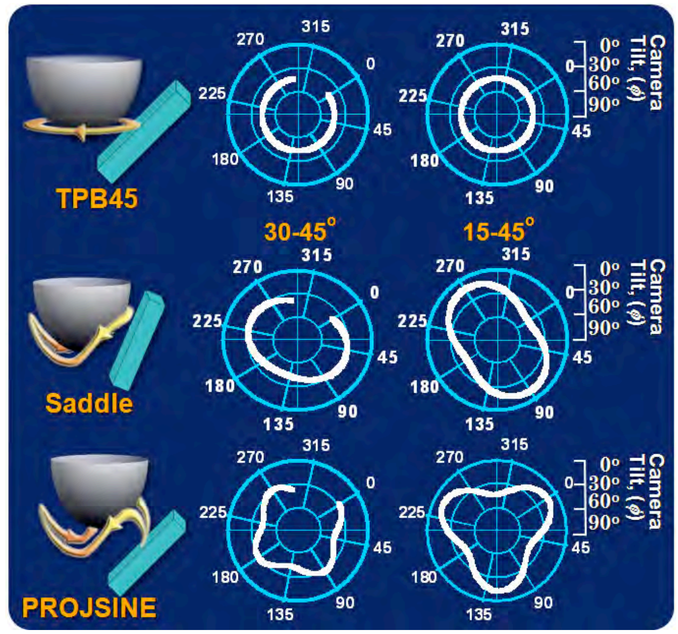

Fig. 4. SPECT acquisition trajectories for the heterogeneous breast phantom studies. Left column shows a 3D illustration of the camera motion. Polar camera tilt as a function of the azimuthal angle is shown for (CENTER COLUMN) reduced angle orbits and (RIGHT COLUMN) full 360^o scans.

total scan time of ~10 minutes per acquisition. Subsequent scans were increased to account for decay.

In the second imaging sequence, the patient bed was raised a few centimeters to allow the tube to rotate fully underneath the head of the patient and CT data were acquired over the full 360^o in 1.5^o increments. The patient bed was then raised again to allow optimal placement of for acquisition of full 360^o TPB45, Saddle, and PROJSINE SPECT scans (Fig. 4, RIGHT COLUMN). Orbits were acquired with 128 projections over 360^o and the total scan time was ~10 minutes.

All other system and reconstruction parameters remained the same as above. SPECT and CT image sets were registered

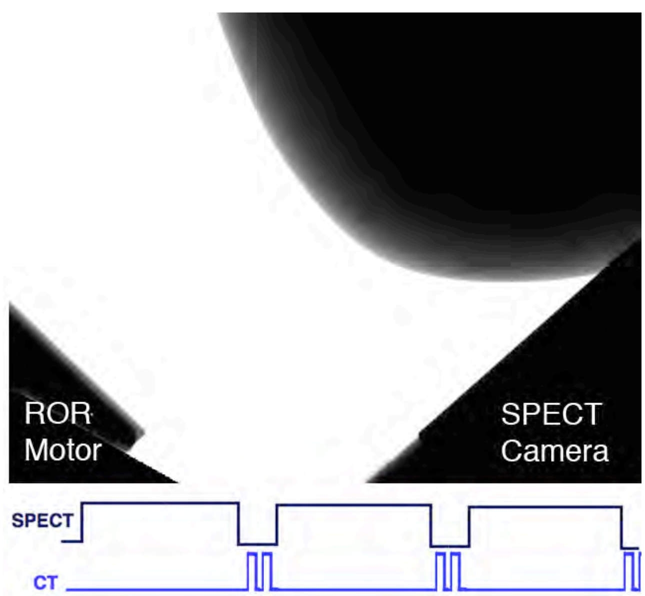

Fig. 5. (TOP) Sample CT projection and (BOTTOM) timing scheme of the interleaved CT scan.

and fused using open source *AMIDE* software [17, 18].

D. Interleaved SPECT-CT

Interleaving the SPECT and CT acquisitions into a single scan was also investigated. The acquisition software was modified such that two rapid CT projections were taken between every five-second SPECT acquisition (Fig. 5). Thus the 3-lobed PROJSINE SPECT orbit was sampled in 3^o increments while the CT sampled in 1.5^o increments over the 360^o scan. Because the SPECT camera sometimes obscures a slight corner of the breast in the CT projections, ~2cm was cropped from either side of projection data, effectively removing the corner where acquired data was obscured as previously described. Both uncropped and cropped data were reconstructed using previously described methods.

E. Modified Patient Bed

A novel concept included in the patient bed was to design the rigid inner octagonal section of the bed to be removable [2]. This center was removed and replaced with a flexible sheet of neoprene layered leaded apron. The weight of the patient naturally protrudes more of her breast into the FOV and the flexible neoprene increases patient comfort by creating a cushioned hammock. Full 360^o dual modality SPECT and CT scans of the same 900mL breast with heterogeneous background were repeated. Lesion-to-background concentration ratios were approximately 10:1. Reconstruction parameters were consistent with earlier parameters, and the reconstructed volumes were fused using *AMIDE*.

III. Results & Discussion

A. Geometric Phantom Study

Reconstructed CT slices of the mini-cold rod data where the central ray was aligned with the COR show minimal distortion even with 180^o of projection data removed (Fig. 6). The smallest sector of rods (1.1mm) is still resolvable with minor cone-beam sampling artifacts beginning to appear on the left edge. Data insufficiency artifacts from the missing projections are much more visually pronounced with the central ray laterally offset 5cm from the COR (Fig. 7). Regions not seen from all 360^o become radially blurred.

For the reconstructed SPECT data, resolution is distance dependant. Even though the cold rods are theoretically fully sampled with 180^o of rotation, objects far from the camera will encounter degraded resolution. Hence a 360^o scan will improve the image resolution. This is qualitatively seen in the SPECT mini-cold rod reconstructions (Fig. 8). The full 360^o images have the highest contrast-resolution. Resolution near the edge of the phantom progressively degrades with decreased angular sampling on that side, as seen in the profiles through the largest 4.7mm rods.

B. Breast Phantom with Homogeneous Background

Resolution degradation is not as immediately apparent in the profiles drawn across the largest lesion of the 900mL

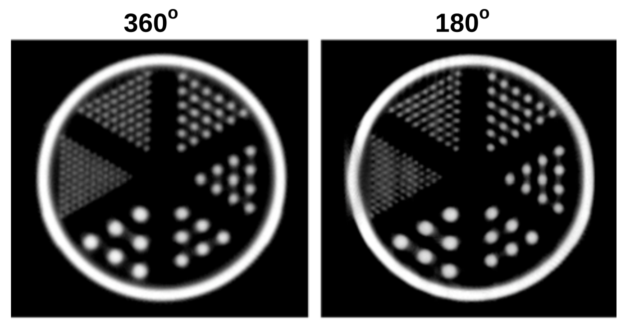

Fig. 6. OSTR iteratively reconstructed CT cold rod data acquired with the central cone-beam ray aligned with the COR. (LEFT) 360^o of projection data. (RIGHT) 180^o of projection data. Three slices were summed to create these images.

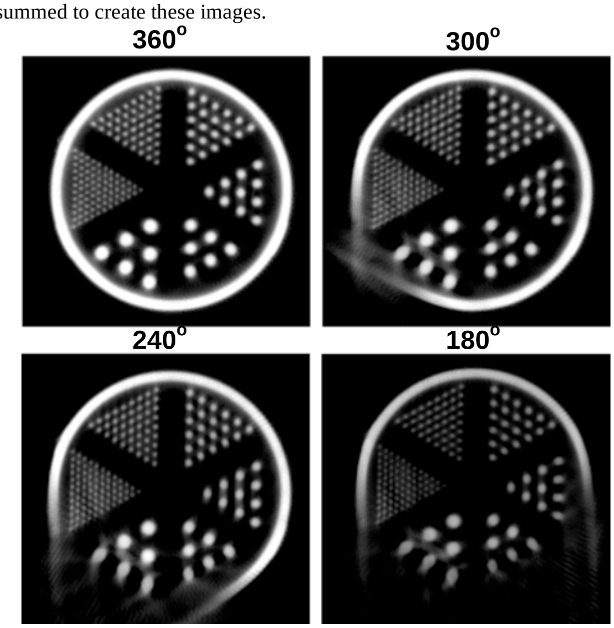

Fig. 7. OSTR Reconstructed CT cold rod data acquired with the central cone-beam ray offset 5cm from the COR. Data insufficiency artifacts become more apparent with decreasing angular sampling.

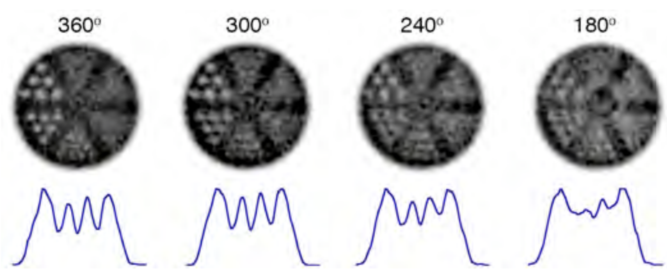

Fig. 8. OSEM reconstructed SPECT mini-cold rod images. Normalized line profiles are shown below, drawn through the largest 4.7mm rods.

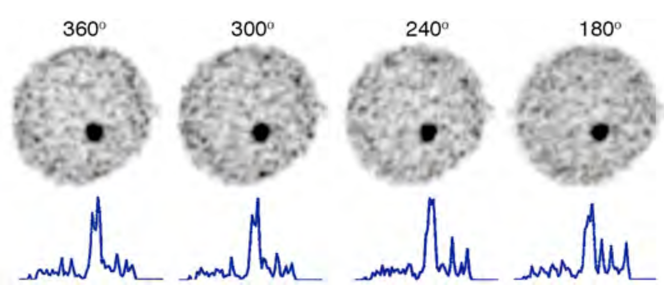

Fig. 9. OSEM reconstructed SPECT breast phantom coronal slices. 2nd iteration shown with 3 summed slices. Normalized line profiles are shown through the 2.3mL lesion.

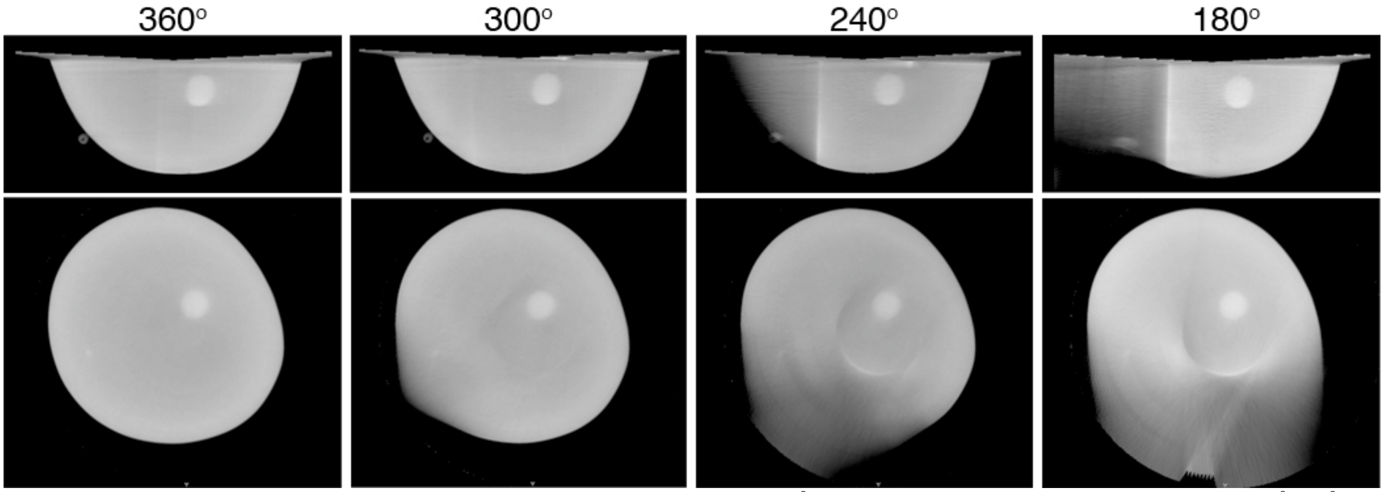

Fig. 10. Reconstructed CT sagittal (TOP) and coronal (BOTTOM) slices. The complete 360^o data are compared with reduced angle scans using 300^o, 240^o, and 180^o of angular sampling. The central cone-beam ray was laterally offset 5cm resulting in truncation artifacts seen in the areas where projection views were not collected.

breast phantom with uniform background (Fig 9). Relative background noise especially on the outer edge of the breast does, however, increase with fewer projections and decreased angular sampling. Both the cold rod and breast data indicate that removing 75^o of SPECT azimuthal data does not significantly reduce image quality.

Reconstructed CT breast images again illustrate artifacts due to incomplete angular sampling (Fig. 10). A distinct loss of attenuation value in the CT reconstructed image on the side where there was no data collected can be measured across the sagittal and coronal slices. In addition, the cylindrical artifacts in the center due to the offset cone-beam became more prominent with decreasing azimuthal acquisition angles.

It is evident from the images of the mini-cold rod and breast phantoms that the lateral offset geometry in our current hybrid system is increasingly penalized when using reduced angle tomography. Disregarding issues of increased scatter, a larger detector with a centrally aligned cone-beam may be a worthwhile solution to avoid truncation of larger breasts for limited angle CT.

C. Breast Phantom with Heterogeneous Background

Truncation artifacts are seen at the bottom of the reconstructed reduced angle SPECT images (Fig. 11). In the current hybrid configuration, the SPECT COR is too near the bottom of the camera face with the bed at the same height as the CT scan. Also because of the limited 30-45^o polar sampling at the low bed height, the air gap between the breast and the heart is less pronounced. Cardiac activity is also more prominent due to more direct views of the heart. In the full 360^o scan, the bed was raised, the polar tilt range of the camera was increased and thus views of the heart were avoided.

In this study the change in polar sampling of the SPECT camera more significantly affected the reconstructed image quality than the reduced azimuthal angular sampling. These results highlight the inherent difficulties in positioning a subject on the bed and the two systems in their current configuration such that the acquisition is simultaneously optimized for both imaging systems. If a universal patient bed height for all of the scans is desired, the SPECT camera needs to be readjusted on the goniometer such that the camera can be positioned to at least 15º polar at the minimum bed height. A single bed height, however, limits the system to a fixed COR and thereby limits the freedom of the SPECT camera. For example, the TPB orbit is more optimal with a lower bed position than the PROJSINE orbit, thus allowing views higher up into the chest and axilla regions.

Fused reconstructed images of the SPECT and CT data illustrate the benefits of combining functional and anatomical information (Fig. 12). The 0.35mL lesion is not more than a suspicious dot in the SPECT images, but its location is verified by the much higher resolution CT images. This lesion, lost in the 360^o scan, also highlights the increased volume seen by the reduced angle scans.

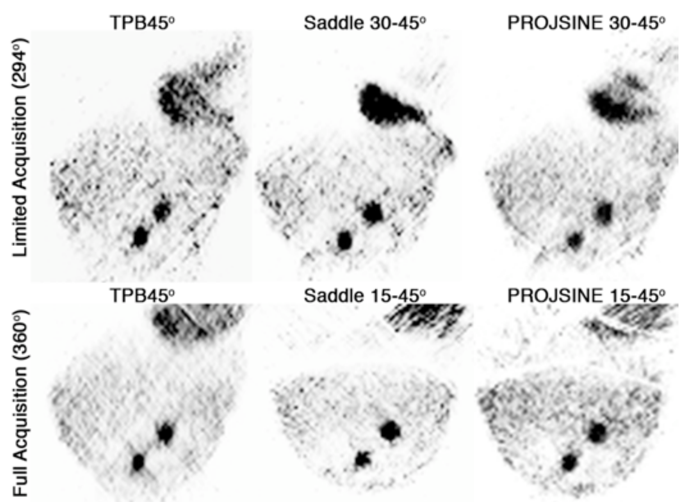

Fig. 11. Sagittal slices of reconstructed SPECT limited angle (TOP) and full 360^o acquisitions (BOTTOM). 2nd iteration is shown with 3 summed slices. 2.3mL lesion is near the center in the breast and 1.0mL lesion is closer to the bottom.

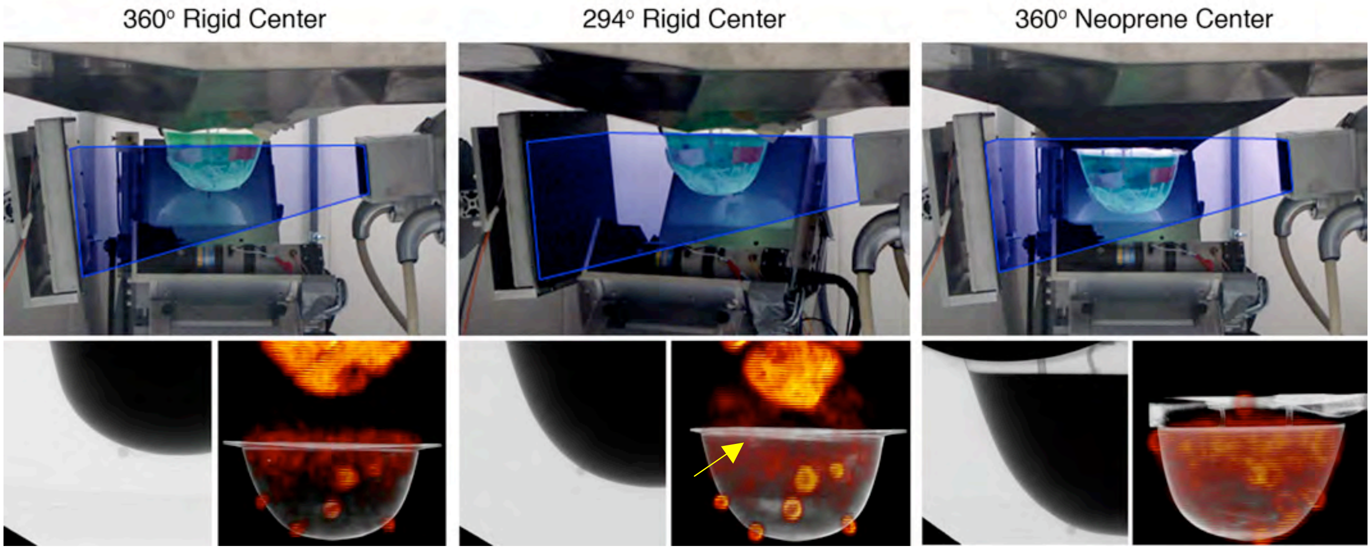

Fig. 12. Breast phantom positioned (TOP LEFT) with bed high enough for 360º clearance, (TOP MIDDLE) with bed lowered to 294º reduced angle scan, and (TOP RIGHT) with flexible center and 360º clearance. Estimated CT cone-beam FOVs are illustrated in blue. Corresponding CT projection data and reconstructed, fused SPECT-CT volume renderings are shown below each system photo. Yellow arrow in bottom center highlights the 3.5mm lesion not seen in the rigid center 360º scan at left. There was no heart activity used in this neoprene study.

D. *Interleaved SPECT-CT*

The reconstructed images of the interleaved SPECT-CT scan are shown in Fig. 13. As expected there are artifacts near the bottom of the breast due to the close proximity of the SPECT camera. The majority of these artifacts are moved outside of the breast after cropping the projection data 2cm on either side. There is no data loss because of the sampling overlap inherent in the lateral offset geometry. The cropped projection data also reduces the cylindrical offset artifact. No measure of increased x-ray scatter off the SPECT camera or SPECT lesion SNR loss was made in this initial investigation.

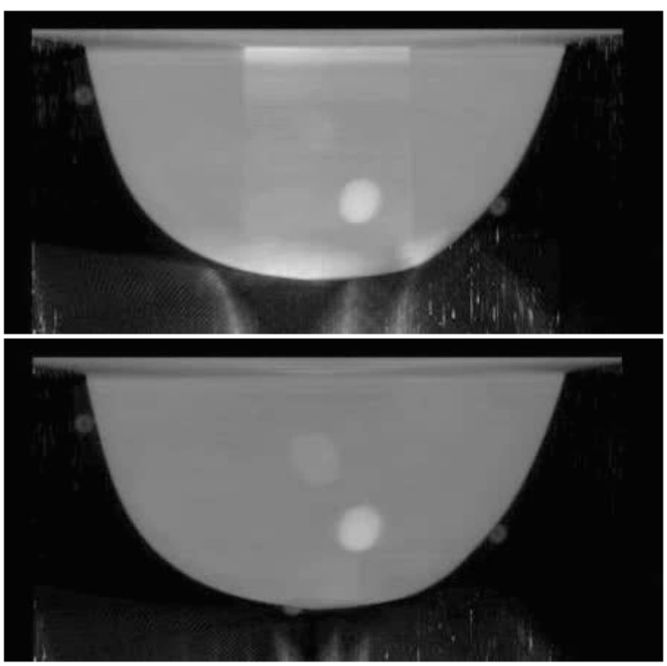

Fig. 13. Volume rendering of iteratively reconstructed CT data acquired in an interleaved fashion with a contouring SPECT scan. Images reconstructed using an (TOP) uncropped and (BOTTOM) cropped

E. *Modified Patient Bed*

Fig. 12 shows projection views and fused reconstructions of all three patient bed-positioning strategies. The patient bed revised with a larger central hole covered with flexible neoprene center clearly allows a dramatic increase in breast volume in the FOV compared to the rigid steel centerpiece, while now regaining the ability to rotate 360^{o} around the breast. The reconstructed CT data visualizes the entire breast volume, including the air gap above the aqueous activity. With the modified bed, the CT cone-beam could potentially image slightly into the chest wall depending on the positioning of the patient.

IV. Conclusions

Reduced angle tomography can be useful for imaging closer to the chest wall while avoiding physical barriers. Both the mini-cold rod and breast data initially indicate that removing 75^{o} of SPECT azimuthal data will not significantly reduce image quality. Observer based studies are warranted to assess clinical viability. CT images were also minimally affected if the cone-beam is centrally aligned with the COR, but dramatically degraded due to aliasing with the laterally offset cone-beam in our current hybrid system. A larger detector with a centrally aligned cone-beam would be a more ideal solution to avoid truncation of larger breasts for reduced angle CT.

Interleaved SPECT-CT scans can speed up and simplify overall scan time, but limit the positioning freedom of the contoured SPECT orbits. The close proximity of the orbiting SPECT camera created artifacts in the CT images which were reduced by cropping the projection data to reduce the overlap region for shifted-CT, where the SPECT camera obscured CT views of the breast. There may be quantitative losses in an interleaved scan that were not investigated in this initial qualitative study. We opted to use separate sequential CT and SPECT scans because the time saved from the interleaved scan did not justify the artifacts in the CT image and limited positioning freedom of the SPECT scan.

The latest patient bed design with flexible center allows more of the breast into the FOV due to a larger hole in the table and natural extension with the weight of the patient. This permits full 360^o dual modality imaging close to and even slightly into the chest wall. With this revised arrangement, the need to image with reduced angle scans may be alleviated.

Acknowledgment

The authors thank Dr. Randy McKinley for technical assistance and suggestions. Martin P. Tornai is the inventor of this technology, and is named as an inventor on the patent for this technology applied for by Duke. If this technology becomes commercially successful, MPT and Duke could benefit financially.

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Appendix C

Empirical Effects of Angular Sampling and Background Content on Image Quality in Dedicated Breast SPECT

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This study investigates the importance and effects of varying the azimuthal and polar sampling of the acquisition trajectory with the dedicated breast SPECT imaging system developed in our lab. In addition, the frequency quality (density and distribution) of the background is considered. The SPECT system consists of a $16x20cm^2$ CZT gamma camera with 6.7% FWHM energy resolution at 140keV, which can accommodate fully 3D simple or complex trajectories about a pendant, uncompressed breast. Various geometric and anthropomorphic phantoms containing lesions are imaged to evaluate the effects of sampling and background distributions on signal (lesion) visualization. In one initial study, two lesions (~0.2 and 0.4ml) are positioned in approximately the same location inside a uniformly filled breast phantom with constant background activity for a variety of angular sampling tests. Evaluated lesion SNR and contrast demonstrated greater effect due to the number of counts per projection than the total number of projections, but this only considered a uniform background signal content. Additionally, azimuthal sampling impacted signal intensity to a greater degree than polar sampling. Additional detailed statistical studies of the angular sampling in the azimuthal and polar directions to characterize the system are underway. Orbits with a variety of projection numbers (64, 128 and 256) and polar tilts (constant, 45° range and 30° range) are being tested with lesions scanned in air and a variety of background activities and density distribution (non-uniform) conditions. In general, sufficient counting statistics limit the quality of the image and thus an optimization between the number of projections and the number of detected events is being explored.

This work was supported by NIH R01-CA096821, DAMD17-03-1-0558, and W81XWH-06-1-0765.

Submitted to the
2007 Nuclear Science Symposium & Medical Imaging Conference
Honolulu, Hawaii
28 October – 3 November, 2007

Appendix D

Initial Patient Study with Dedicated Dual-Modality SPECT-CT Mammotomography

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Dual-modality SPECT-CT dedicated breast imaging offers great promise in imaging normalcy and detecting and staging disease in the breast, monitoring treatment therapies, and improving surgical biopsy guidance. Independent SPECT and CT subsystems have been integrated onto a single gantry with a common FOV for pendant, uncompressed breast imaging. The SPECT system consists of a $16x20cm^2$ CZT gamma camera having 6.7% FWHM energy resolution at 140keV. The camera is attached to a rotation stage and goniometer such that customized trajectories can be used to acquire data in close proximity to the suspended breast. The CT component includes a heavily K-edge filtered W-target x-ray source yielding a quasi-monochromatic cone beam, and has a $20x25cm^2$ CsI(T1) digital detector having high efficiency for low energy x-rays. The CT system is restricted to simple circular motion around the pendant breast. Iteratively reconstructed breast phantom studies using fiducial markers demonstrate fused functional-anatomical images of high quality. In the first dedicated patient study, a cancer-positive volunteer was SPECT scanned lying prone with her breast suspended through a cutout on a customized radio-opaque patient bed placed over the system. There was a clearly enhanced, detailed volume of tracer uptake in the anterior chest wall, corresponding to the known lesion seen in the contrast enhanced MRI breast scan. While out of field background activity was minimized due to the use of a radio-opaque bed, streak artifacts and additional enhanced regions appear posterior to the breast, due to the cardiac-hepatic uptake of tracer. Further hybrid SPECT-CT patient studies are in progress. This compact dual modality system is capable of non-invasively providing complementary functional and anatomical fully-3D activity distribution information of the breast, and has the potential to help further enhance the visual and quantitative information over the independent systems.

This work was supported by NIH R01-CA096821, and in part by DOD W81XWH-06-1-0791, W81XWH-06-1-0765, W81XWH-05-1-0280, and DAMD17-03-1-0558.

Presented at the
2007 Nuclear Science Symposium & Medical Imaging Conference
Honolulu, Hawaii
28 October – 3 November, 2007

Appendix E

Automation and Preclinical Evaluation of a Dedicated Emission Mammotomography System for Fully 3-D Molecular Breast Imaging

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Our lab has developed a novel single photon emission computed tomography (SPECT) system for uncompressed dedicated molecular breast imaging. Using a compact, high performance gamma camera, the versatile positioning gantry allows for fully 3D imaging anywhere within a hemispherical volume about the pendant breast, and overcomes physical proximity restrictions of standard clinical gamma cameras or compact systems without 3D motion (Fig. 1).

The overall objective of this proposal is to fully automate and optimize the performance of the system for enhanced semi-automated clinical testing. A retrospective study of 103 clinical MRI uncompressed breast scans was conducted to analyze how to adapt existing SPECT acquisition orbits for varying breast shapes (Fig. 2). A database of pendant breast measurements and surface renderings was compiled. The wide variety of breast volumes and shapes observed reinforce the need to automate the radius of rotation component of the SPECT orbit. Laser ribbon ranging sensors and associated hardware to fully automate the radius of rotation were acquired and successfully bench tested. Software and hardware system implementation are currently in progress.

An observer based 3D contrast-detail study was performed in an effort to evaluate the limits of object detectability for the system under various imaging conditions. A novel, geometric contrast-resolution phantom was developed that can be used for both positive (hot) and negative contrasts (cold). Results show little statistically significant difference ($p<0.05$) between simple vs. complex trajectories or whether phantom rods appeared hot or cold, indicating that data acquisition with the system is quite robust. We anticipate that fully automated molecular breast imaging will improve detection and potentially *in vivo* characterization of early stage breast cancer.

Presented at the

2008 Era of Hope Meeting

Baltimore, Maryland

25 – 28 June, 2008

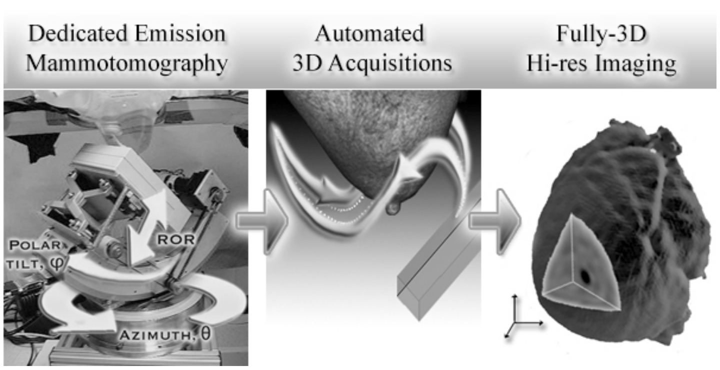

Figure 1: Dedicated Emission Mammotomography

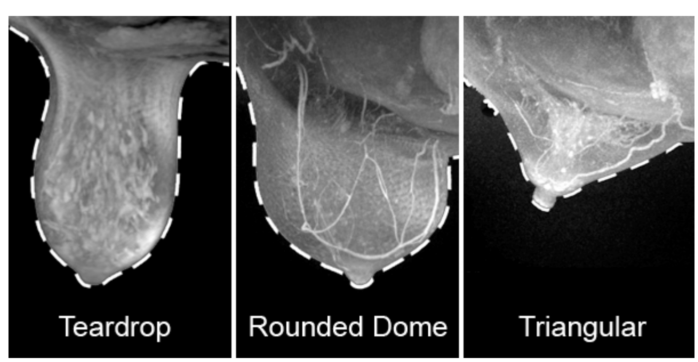

Figure 2: Sample Breast MRI images and shape classifications

Appendix F

Dedicated Molecular and Anatomical Breast Imaging - Initial Patient Studies

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Breast cancer is the most commonly diagnosed cancer among women worldwide and is the second leading cause of cancer death in the US. With the limitations and discomfort of mammography, alternative imaging techniques to detect and monitor breast cancer early, reduce unnecessary biopsies, and improve patient comfort have been designed. We have developed a compact, dedicated, dual-modality SPECT (single photon emission computed tomography - a molecular imaging approach) and CT (computed tomography - a diagnostic imaging approach) system, which allows for quantitative 3D volumetric functional and anatomical imaging, respectively, of a pendant, uncompressed breast. Fused images can potentially provide more valuable clinical information for evaluation of cancerous diseases than the independent systems alone. A preliminary investigation on the clinical performance of the hybrid system was done by imaging women with biopsy confirmed breast cancer. With no breast compression and an open, common field-of-view geometry system, the patient lies prone on a customized patient bed while the hybrid device non-invasively acquires 3D data underneath. Using the flexible positioning capability of the gantry, the SPECT subsystem acquires data using a 3D complex trajectory, which permits the camera to get closer to the breast and chest wall. CT images were collected with the system rotating circularly around the breast. Initial human subject studies demonstrated that SPECT images can clearly visualize the tracer uptake by the tumor, and the subsystem has the capability to view into the chest wall. Physical system constraints limited visualization of the chest wall in the CT images. With the elimination of overlapping tissues through 3D imaging, CT images can potentially improve lesion isolation versus conventional screening modalities. Future studies include improved patient positioning for better CT chest inclusion as well as clinical comparisons with mammograms and/or MRI images for quantification of potential improved detection.

Grant Support: NIH Grant R01-CA096821, and
DOD Predoctoral Awards: DAMD17-03-1-0558, W81XWH-05-1-0280, W81XWH-06-1-0765, W81XWH-06-1-0791, W81XWH-08-1-0192, and W81XWH-08-1-0352

Presented at the
50th Annual Meeting of the American Association of Physicists in Medicine,
Houston, TX
27-31 Jul. 2008